## DETAILED ACTION

A response and amendment were received and entered on July 21, 2005. All evidence and arguments have been fully considered. Claims 21-25 were cancelled. Claims 26-33 are pending and examined on the merits in this office action.

### *Claim Rejections - 35 USC § 112*

1. Rejections under 35 USC 112 have been withdrawn due to amendment.

### *Claim Rejections - 35 USC § 101*

2. Rejections under 35 USC 101 have been withdrawn due to amendment.

### *Claim Rejections - 35 USC § 102*

3. Rejections under 35 USC 102 have been withdrawn due to amendment.

### *Claim Rejections - 35 USC § 103*

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 26-28, 32 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eschenfelder et al. (US 4,944,943) in view of Baldwin (US 5,098,707, cited in prior action). The claims recite a method for treating hemorrhoid disease in a human in need thereof, comprising administering to said human an effective amount of a pharmaceutical composition, said composition comprising a thrombolytic protein selected from the group consisting of tissue-type plasminogen activator (t-PA), urokinase (u-PA), streptokinase (SK), or a combination thereof. Further claimed embodiments include that the pharmaceutical composition comprises recombinant SK and a carrier or excipient, wherein the concentration of SK is 50,000 to 1,500,000 IU per gram of pharmaceutical composition, and that the composition is administered rectally, specifically as a suppository.

8. Baldwin teaches compositions comprising streptokinase for the treatment of vascular disease (abstract; col. 1, lines 34-46, col. 24, lines 1-35). Baldwin teaches that these compositions may be formulated in rectal compositions, such as suppositories, containing a carrier that is pharmacologically acceptable for rectal administration (col. 24, lines 32-35). Baldwin teaches that the streptokinase that is used in the composition may be of recombinant origin (col. 4, lines 8-17). Baldwin teaches that 1,500,000 units of streptokinase may be used in the composition (col. 24, lines 13-19). The reference does not disclose the use of the composition for the treatment of hemorrhoid disease.

9. Eschenfelder teaches a method for the treatment of vascular disorders, such as hemorrhoid disease, comprising administering a thrombolytic substance such as streptokinase to a patient (col. 1, lines 26-36, col. 2, lines 21-41).

10. At the time of the invention, a method of treating vascular diseases such as hemorrhoid disease using a composition comprising streptokinase was known, as taught by Eschenfelder. It was further known that streptokinase-containing compositions for the treatment of hemorrhoid diseases could be administered using the claimed conditions (i.e., as a suppository). One of ordinary skill in the art would have been motivated to combine these teachings because Eschenfelder teaches that the addition of an antithrombotic agent to the composition makes the composition suitable for a wider variety of purposes (col. 2, lines 21-41). Further, one of ordinary skill in the art would have recognized that the amount taught by Baldwin could be used and varied over the course of routine experimentation to arrive at a composition with the claimed amount of streptokinase. One of ordinary skill in the art would have had a reasonable

expectation of success in combining these teachings because both teach the manufacture of a composition comprising streptokinase that is suitable for use with multiple carriers. It would therefore have been obvious to one of ordinary skill in the art to combine the teachings discussed above to arrive at the claimed invention.

11. Claims 26-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eschenfelder et al. (US 4,944,943) in view of Baldwin (US 5,098,707, cited in prior action) as applied to claims 26-28, 32 and 33 above, and further in view of Ivy (US 5.720,962) and Oh (WO 01/22935 A1). The claims recite a method for treating hemorrhoid disease in a human in need thereof, comprising administering to said human an effective amount of a pharmaceutical composition, said composition comprising a thrombolytic protein selected from the group consisting of tissue-type plasminogen activator (t-PA), urokinase (u-PA), streptokinase (SK), or a combination thereof. Further claimed embodiments include that the pharmaceutical composition comprises recombinant SK and a carrier or excipient, wherein the concentration of SK is 50,000 to 1,500,000 IU per gram of pharmaceutical composition, that the composition further comprises EDTA, sodium diclofenac, or sodium salicylate, and that the composition is administered rectally, specifically as a suppository.

12. Baldwin teaches compositions comprising streptokinase for the treatment of vascular disease (abstract; col. 1, lines 34-46, col. 24, lines 1-35). Baldwin teaches that these compositions may be formulated in rectal compositions, such as suppositories, containing a carrier that is pharmacologically acceptable for rectal administration (col.

24, lines 32-35). Baldwin teaches that the streptokinase that is used in the composition may be of recombinant origin (col. 4, lines 8-17). Baldwin teaches that 1,500,000 units of streptokinase may be used in the composition (col. 24, lines 13-19).

13. Eschenfelder teaches a method for the treatment of vascular disorders, such as hemorrhoid disease, comprising administering a thrombolytic substance such as streptokinase to a patient (col. 1, lines 26-36, col. 2, lines 21-41).

14. As discussed above, it would have been obvious to combine the teachings of Baldwin and Eschenfelder to arrive at nearly all of the elements of the claimed invention. Neither of the reference, however, teaches a composition comprising EDTA, sodium diclofenac, or sodium salicylate.

15. Ivy and Oh both teach compositions for the treatment of hemorrhoid disease. Ivy teaches compositions comprising EDTA (abstract, col. 2, lines 21-25) and Oh teaches compositions comprising salicylic acid and diclofenac (p. 5, lines 26-35, p. 3, lines 5-25).

16. For the reasons discussed above, a method of treating hemorrhoid disease comprising nearly all of the claimed elements would have been obvious at the time of the invention, as taught by Eschenfelder and Baldwin. It was also known at the time of the invention that EDTA, salicylic acid, and diclofenac were pharmaceutically acceptable additives to compositions for the treatment of hemorrhoid disease. One of ordinary skill in the art would have been motivated to add these components for a composition for carrying out the claimed method because Baldwin teaches that the compositions may contain other pharmaceutically accepted ingredients (col. 24, lines 20-41). There existed at the time of the invention a finite number of predictable

potential additives to a composition for use in a method of treating hemorrhoid disease, including the additives taught by Ivy and Oh. One could have used these additives with a reasonable expectation of success because all of the references teach that the compositions were suitable for use in a method for the treatment of hemorrhoid disease. It would therefore have been obvious to combine the teachings discussed above to arrive at the claimed method.

17. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

### ***Response to Arguments***

18. Applicant's arguments with respect to cancelled claims 21-25 have been considered but are moot in view of the new ground(s) of rejection.

### ***Conclusion***

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHERIDAN R. MACAULEY whose telephone number is (571)270-3056. The examiner can normally be reached on Mon-Thurs, 7:30AM-5:00PM EST, alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon B Lankford Jr/
Primary Examiner, Art Unit 1651

SRM